Author’s response to reviews

Title: Predictive characteristic of simple bone cyst treated with curettage and bone grafting.

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To the “BMC Musculoskeletal Disorders” Editor James Mockridge

On behalf of my co-authors, I am submitting to you the paper entitled ‘Types of simple bone cyst that could be effectively treated with curettage and bone grafting’ by Flont P, Malecki K, Niewola A, Lipczyk Z, Niedzielski K for possible publication as a research paper.

This paper shows that cyst treated with curettage, correlations were identified between worse treatment results and the location in the humerus, pathological fractures at the time of diagnosis, large cyst area, large cyst index and large cyst diameter.

I confirm that all co-authors as well as the responsible authorities at our institution approved the manuscript and that it has not been submitted previously to another journal or published elsewhere. Our investigation have been carried out in accordance with the Helsinki Declaration (1964).

We agree, if and when the manuscript is accepted for publication, to automatic and free transfer of copyright to the Publisher allowing for the publication and distribution of the material submitted in all available forms and fields of exploitation. We accept that the manuscript will not be published elsewhere in any language without the written consent of the copyright holder, i.e. the Publisher.

I hope reviewers will find it suitable for publication in the “BMC Musculoskeletal Disorders”.
Yours sincerely,

Pawel Flont

Answers for Reviewers

Reviewer 1.

1) First of all the title 'Types of simple bone cyst that could be effectively treated with curettage and bone grafting.' does not reflect the study. Hence, authors studied on predictive characteristics of SBC I suggest new title which will totally contain the aim of the study

We have changed the title:

“Predictive characteristic of simple bone cyst treated with curettage and bone grafting.”

2) Special Topics: 1- Please give the results in results section instead of materials and methods in abstract section

The results have been moved to the appropriate section.

Results

“No statistically significant differences regarding age, sex or type of bone graft (p > 0.05) were found.”

2) 2- Authors wrote same sentence and same mistake ( Neer stages 1 and 2 and NERR Stages.....) in three different section which means copy and paste.

The name of the Neer scale has been corrected where necessary.

3) 3- Page 4 line 103: Authors constitute new group (1,2,3) but not discussed the results according to group anywhere. What is the importance of this group.

The ratio of longitudinal bone axis length to cyst length has been removed. This ratio was used in earlier SBC studies but has since lost any clinical or scientific importance.

4) 4- Page 4 line 118: 'UBC' please indicate UBC.

The term UBC (unicameral bone cyst) has been changed to SBC (simple bone cyst) to avoid confusion for the reader.

5) 5- Page 5 lines 146-147: The curettage procedure was significantly more likely to fail when the cyst was located in the humerus. Please discuss the possible reasons and treatment strategies for failed humerus SBC in discussion section. Please add some figures showing recurrence and after treatment humeral SBC
We explain our prediction why curettage in humerus is more likely to fail.

“In the humerus, the SBC are usually larger with thinner walls than those in other locations. Due to their asymptomatic course, they are diagnosed after first fracture. In our opinion, the higher recurrence rates observed following this more technically demanding curettage can be attributed to the large size, thin wall and irregularity of cortical layers after fracture.”

We have added a few examples recurrences after curettage (with Figures) which was treated with steroid injection or with titanium intramedullary nailing.

6) Page 7 lines 240-242: In the group treated with curettage, correlations were identified between worse treatment results and the location in the humerus, pathological fractures at the time of diagnosis, large cyst area, large cyst index and large cyst diameter. Do the authors have some critical values for 'large cyst index and diameter'. How large ?. And again there is contrast with title and conclusion (Positive response X Recurrence)

Our results indicate that radiological parameters (such as cyst area, cyst index and cyst diameter ratio) vary significantly between groups. Unfortunately, critical values are not available; however, mean ratio and standard deviation for these parameters are given in Table 3.

We have changed the sentences:

“The conclusion is that curettage with a graft procedure is indicated at patients with SBS in locations other than humeral bone with no pathological fractures, or a lower cyst area, cyst index or cyst diameter ratio”.

“In the group treated with curettage, correlations were identified between worse treatment results and the location in the humerus, pathological fractures at the time of diagnosis, larger cyst area, larger cyst index and larger cyst diameter”.

Reviewers 2.

1) I found it peculiar that the authors commenced their Results section with their recurrence and complication data. One would normally broadcast one's successes first.

We have removed part of study about recurrences and complications to the end of results paragraph.

2) I think the results section needs to be re-written and restructured; as does the Results section in the Abstract

We have restructured the Results section.

Abstract
Results

“Significantly fewer patients with lesions located in the humerus (chi2=9.351; p <0.05) and without pathological fracture at the time of diagnosis (p=0.017) were found in the group with no recurrence. The following radiological parameters were found to vary significantly between groups: cyst area (z=3.121; p<0.01), cyst index (z=2.213; p <0.05) and cyst diameter ratio (z=2.202; p <0.05). In the group with no recurrences, the mean values of these parameters were found to be lower than in group with poor response to treatment. No statistically significant differences regarding age, sex or type of bone graft (p > 0.05) were found. Recurrences were experienced by 10 patients (41.7%) during the 3-year period after surgery.”

3) They then go on to discuss how these recurrences were managed, which was not really within the remit or objectives of the study. To hen state that all their revision surgery was successful then undermines any string conclusion about their original treatment methodology (ie maybe actually bone grafting and curettage does not work - 40% failure rates, while methylpred and fibular grafting with en bloc excision works without fail). I would leave out the section about how the revisions were managed, completely

We have not completely removed the section about how the revisions were managed because other reviewers recommended we emphasise it and add figures. Therefore, as a compromise, it has been shortened and placed in the end of the Results section.

“Recurrences were experienced by 10 patients (41.7%) during the 3-year period after surgery. In treating recurrences, the following techniques were used: methylprednisolone injection (7 patients, Fig.1), en bloc excision followed by transplantation of autogenic fibular grafts (large cysts, 2 patients) and titanium intramedullary nailing (1 patient, Fig. 2). The follow-up revealed limb length discrepancy in 4 patients (16.7%) and pathological fractures were observed in 4 patients (16.7%): 2 cases of humeral cysts, 1 case of an intertrochanteric cyst and 1 case of a cyst in the distal tibia.”

4) It would be interesting for the authors to comment on why they treated their cases with just curettage and grafting, rather than with additional chemical resection. when recurrence rates are so much greater and this has been known from the literature for some time. 40% vs 15% respectively in the 1980s. They achieved similar results in 2000s.

We did not use additional chemical resection because this procedure has been discredited. In the 80s, some authors suggest that additional resection (phenol, zinc dioxide) leads to more pathological fracture and infection rate. It is now known to possibly lower the rate of recurrence without complication in benign bone tumor surgery (especially liquid nitrogen and argon beam). Nowadays, in our clinic, cryosurgery or argon beam treatment is used for all bone surgery, and this has been available in our clinic for 5 years. This study was conducted earlier and was performed to indicate predictive factors. We believe that the predictive factor can be the same for curettage or for a combination of this procedure with additional chemical resection.

5) Despite statistical analyses it is difficult to draw true conclusions about which cysts should be treated by curettage and grafting, when their results are similar to those in the
literature in which others papers report on diverse populations of patients with diverse cyst locations, with similar outcomes (which might suggest that factors other than those analyzed may also be in play).

We deleted the conclusions

“Hence, it is necessary to define adequate indications for this type of surgery. This study identifies the characteristics of cysts which should be treated with curettage and grafting: location other than the humeral bone, small cyst area, low cyst index, low cyst diameter ratio and lack of any fracture.”

6) Lines 159-161. Conclusions should not be in the Results section!

We deleted the conclusions given in the Results section.

“The conclusion is that curettage with a graft procedure is indicated at patients with SBS in locations other than humeral bone with no pathological fractures, or a low cyst area, cyst index or cyst diameter ratio.”

7) Some of the Discussion is repetitive and could be cut down significantly. Also the commentary about the techniques the clinic is using in the 2010s is not relevant to the paper. Are they writing about their case series or about different patients. Lines 188-195 should be removed entirely. Lines 198-203 are already in the Introduction and do not need to be repeated Lines 204-207 do not relate to the cases in this series or the technique that was used, and should be removed.

We cut down the Discussion and deleted the following sentences.

“Although cyst curettage is one of the first known ways of treating SBC in children, no precise qualification criteria exists for this procedure. The application of this technique has recently been limited because of the development of less invasive procedures. Unfortunately, new techniques are also connected with a high percentage of recurrence and prolonged healing time. Nowadays our clinic performs curettage and grafting of SBC in only 20% of patients, with less invasive procedures, such as steroid injections, bone marrow stem cells concentrate injection, intramedullary stabilization or applying such osteoconductive materials as hydroxyapatite or tricalcium phosphate, being performed in other patients. Curettage is performed in following cases: a) recurrences, b) lesions with a safe surgical approach, c) lesions of no certain character (after imaging diagnostic – CT, MRI, biopsy) or d) in the case of incertainty between simple cyst or aneurysmal cyst (especially in children younger than 5 years old). This procedure is followed by the cavity being filled with allo- or autogenic bone grafts. As taking autogenic bone grafts from the iliac crest in children is limited, especially younger ones, and it can cause some serious pain or even growth disturbances, it is preferable to use allogenic bone grafts [25]. During curettage, care is taken to completely remove all cyst walls and open the medullar canal.

Due the lack of knowledge regarding etiology, there is no agreement on how and when to treat simple bone cysts. The most commonly performed treatment option is injecting substances such
as steroids [10], biologically active (osteoinductive) substances including bone marrow concentrate, platelet derived growth factors or DBM [13,14], or osteoconductive substances such as hydroxyapatite, calcium phosphate pellets, calcium phosphate, or calcium sulphate-calcium phosphate composite [15,26]. Additionally, cyst decompression with medullar canal opening can be performed (ESIN, cannulated screws or multiple drilling) [11,12].

Treatment with osteoinductive and osteoconductive materials for a short period of time does not influence the mechanical properties of bone. The bone rebuilding period is long, and for complete cyst healing, several procedures could be required. In the rebuilding period, limiting physical activity could be necessary to prevent pathological fracture. In justified cases, low-invasive procedures should be connected with prophylactic intramedullary stabilization – especially in the lower limbs with greater risk of pathological fracture [21,22,27,28]. A risk of fracture exists if the bone cyst index>3.5, bone cyst diameter>85%, and the minimal cortical thickness<1 mm [29].”

8) I think that the paper is interesting, but the conclusions cannot be drawn strongly. All one can say is that there are association between the analysed factors (no causative link).

We deleted conclusion and write only about association between factors.

Deleted sentences.

“The curettage procedure was significantly more likely to fail when the cyst was located in the humerus.”

“This statistical correlation implies that pathological fracture is a negative predictive factor.”

“This implies that a positive response to curettage with graft surgery is more probable in smaller lesions.”

We change the conclusion.

“In the group treated with curettage, associations were identified between worse treatment results and the location in the humerus, pathological fractures at the time of diagnosis, large cyst area, large cyst index and large cyst diameter”.